Factors influencing multiple imputation in longitudinal ordinal data

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Annual meeting SBS-BVS
Liège, 25 October 2012

Outline of the presentation

- Introduction
- Multiple imputation (MI-GEE)
  - Monotone
  - Non-monotone
- Simulation plan
- Results
  - Monotone
  - Non-monotone
- Conclusions

Analysis of ordinal longitudinal data

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Solution Use **Multiple Imputation (MI)** as a preliminary step

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1. Imputation stage - $Y_{ij}^{mis} \Rightarrow Y_{ij}^{1}, \cdots, Y_{ij}^{M}$
2. Analysis stage - Analyze the M completed datasets using GEE

$$\left(\hat{\beta^{m}}, \hat{var}(\hat{\beta^{m}})\right), m = 1, \cdots, M$$

3. Pooling stage - Combination of the M results

$$\hat{\boldsymbol{\beta}}^{*} = \frac{1}{M}\sum_{m=1}^{M}\hat{\boldsymbol{\beta}}_{m} \quad \mathbf{T} = \mathbf{W} + \left(1 + \frac{1}{M}\right)\mathbf{B}$$

where $\mathbf{W} = \frac{1}{M}\sum_{m=1}^{M} \hat{var}(\hat{\beta^{m}})$ and $\mathbf{B} = \frac{1}{M-1}\sum_{m=1}^{M}(\hat{\boldsymbol{\beta}}_{m} - \hat{\boldsymbol{\beta}}^{*})(\hat{\boldsymbol{\beta}}_{m} - \hat{\boldsymbol{\beta}}^{*})'$

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Imputation mechanism

Let $\boldsymbol{\theta}$ represents the parameter vector of the distribution of the response $\mathbf{Y}$. The idea is to impute missing data using $f(\mathbf{Y}^{mis}|\mathbf{Y}^{o}, \boldsymbol{\theta})$.

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Imputation mechanisms based on :

- Multivariate Normal Imputation (MNI)

- Ordinal (logistic regression) Imputation Model (OIM)

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2. **P-step** New value for the mean and the covariance , $\hat{\boldsymbol{\theta}}_{(j)}$, are simulated by drawing from their posterior distribution.

Both steps are iterated long enough to provide a stationary Markov chain $(\mathbf{Y}^{mis}_{(1)}, \boldsymbol{\theta}_{(1)}), (\mathbf{Y}^{mis}_{(2)}, \boldsymbol{\theta}_{(2)}), \cdots$. The last iteration is used to impute $\mathbf{Y}^{mis}$ in the dataset.

Repeat to obtain M sets of imputed values.

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Problem when applied to ordinal data

- Normality assumption fails
- Imputed values are no longer integers between 1 and K $\rightarrow$ rounding

Imputation methods - OIM

Ordinal imputation model:

$$logit[Pr(Y_{ij} \leq k)|\mathbf{x}_{ij}^{*}] \quad = \quad \gamma_{0k} + \mathbf{x'}_{ij}^{*}\gamma \qquad (1)$$

where the covariates typically include $\mathbf{X}_{ij}$, possible auxiliary covariates $\mathbf{A}_{ij}$, and the previous outcomes $\tilde{\mathbf{Y}}_{ij} = (Y_{i1}, ..., Y_{i,j-1})$.

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   where $\mathbf{V}_{hi}$ is the upper triangular matrix of the Cholesky decomposition of $V(\hat{\mathbf{\Gamma}})$ and $\mathbf{Z}$ is a $[(K-1)+q]-$vector of independent random Normal variates.

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Application of OIM depends on the missingness pattern.

Imputation methods - OIM - Monotone

X	Y_1	$\cdots$	Y_{j-1}	Y_j	Y_{j+1}
O	O	$\cdots$	O	O	O
O	O	$\cdots$	O	O	O
O	O	$\cdots$	O	O	M
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O = observed - M = missing

$\xrightarrow[\text{OIM}]{\text{sequential}}$

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In this way, the part of the dataset used to impute Y_j is only composed of observed values for all previous variables $(Y_1, \cdots, Y_{j-1})$. So, $\hat{\mathbf{\Gamma}}_j$ do not depend on any previous imputed values, which means that $\hat{\mathbf{\Gamma}}_j$ is independent of $\hat{\mathbf{\Gamma}}_1, \cdots, \hat{\mathbf{\Gamma}}_{j-1}$, monotone-distinct structure (Rubin, 1987).

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In this way, the part of the dataset used to impute Y_j may be composed of observed and imputed values. So, $\hat{\boldsymbol{\Gamma}}_j$ are derived using previous imputed values and are therefore dependent on $\hat{\boldsymbol{\Gamma}}_1, \cdots, \hat{\boldsymbol{\Gamma}}_{j-1}$.

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$\Rightarrow$ **Fully conditional specification** (FCS, (Van Buuren, 2006)) using OIM.

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- To stabilize the results (independence of initial values), the sequential imputation of the dataset is iterated.

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Simulation plan

Longitudinal ordinal data model:

$$\text{logit}[\Pr(Y_{ij} \leq k|x_i, t_j)] = \beta_{0k} + \beta_x x_i + \beta_t t_j + \beta_{tx} x_i t_j \quad (k = 1, \cdots K - 1)$$

with a binary group effect ($x = 0$ or 1), an assessment time (t) and an interaction term between group and time.

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MAR missingness generation: monotone

$$\text{logit}[\Pr(Drop_i = j | x_i, Y_{i,(j-1)})] = \psi_0 + \psi_x x_i + \psi_{prev} Y_{i,(j-1)}$$

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Model simulation parameters (Well-balanced data):
$K = 2, 3, 4, 5$ and 7
$T = 3, 5$
$N = 100, 300, 500$
Missingness $= 10\%, 30\%, 50\%$
$\rightarrow$ 90 different combination patterns. For each pattern, 500 random samples were generated.

Simulation results - **monotone**

Relative bias (%)

Relative bias (Mean ± SD)

	MNI	OIM	Difference
β_x	89.4 ± 13.1	99.5 ± 15.5	-10.1 ± 8.91
β_t	84.6 ± 10.4	100.9 ± 8.95	-16.4 ± 9.58
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Simulation results - **monotone** - Relative bias β_{tx}

Number of levels K

K	MNI	OIM	Difference
2	92.9 $\pm$ 5.18	101.2 $\pm$ 2.93	-8.35 $\pm$ 4.29
3	94.1 $\pm$ 2.98	103.4 $\pm$ 4.23	-9.35 $\pm$ 4.34
4	88.0 $\pm$ 6.71	99.1 $\pm$ 6.05	-11.1 $\pm$ 4.66
5	89.1 $\pm$ 5.36	99.5 $\pm$ 3.09	-10.4 $\pm$ 4.70
7	88.7 $\pm$ 5.56	95.0 $\pm$ 6.12	-6.34 $\pm$ 3.87
	< 0.0001	< 0.0001	0.034

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Number of time points T

T	MNI	OIM	Difference
3	91.7 ± 5.82	100.9 ± 5.34	-9.26 ± 4.73
5	89.4 ± 5.47	98.4 ± 5.14	-8.94 ± 4.51
	0.007	0.009	0.61

Simulation results - **monotone** - Relative bias β_{tx}

Sample size

N	MNI	OIM	Difference
100	90.5 $\pm$ 6.60	97.7 $\pm$ 6.73	-7.22 $\pm$ 4.18
300	90.9 $\pm$ 5.37	100.8 $\pm$ 4.77	-9.88 $\pm$ 4.48
500	90.2 $\pm$ 5.29	100.4 $\pm$ 3.85	-10.2 $\pm$ 4.67
	0.74	0.027	0.0002

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	0.74	0.027	0.0002

Rate of missingness

Missingness	MNI	OIM	Difference
10%	95.4 ± 2.65	100.1 ± 2.47	-4.64 ± 0.94
30%	89.9 ± 3.23	99.9 ± 3.57	-9.94 ± 2.21
50%	86.3 ± 6.29	99.0 ± 8.31	-12.7 ± 4.92
	< 0.0001	0.37	< 0.0001

Conclusions - **monotone**

Relative bias

- MNI yields highly underestimated model parameters
- The estimates derived under the OIM method are almost unbiased.

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		K	N	T	Missingness
β_x	MNI			$\uparrow$	
	OIM	$\uparrow$	$\downarrow$	$\uparrow$	
β_t	MNI	$\uparrow$			$\uparrow$
	OIM	$\uparrow$	$\downarrow$	$\uparrow$	
β_{tx}	MNI	$\uparrow$		$\uparrow$	$\uparrow$
	OIM	$\uparrow$	$\downarrow$	$\uparrow$	

$\uparrow$ Absolute bias increases

$\downarrow$ Absolute bias decreases

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		K	N	T	Missingness
β_x	MNI			$\uparrow$	
	OIM	$\uparrow$	$\downarrow$	$\uparrow$	
β_t	MNI	$\uparrow$			$\uparrow$
	OIM	$\uparrow$	$\downarrow$	$\uparrow$	
β_{tx}	MNI	$\uparrow$		$\uparrow$	$\uparrow$
	OIM	$\uparrow$	$\downarrow$	$\uparrow$	

$\uparrow$ Absolute bias increases

$\downarrow$ Absolute bias decreases

MSE

- MNI and OIM were similar

Simulation results (preliminary) - **non-monotone**

Relative bias (%)

Relative bias (Mean ± SD)

	MNI	FCS OIM	Difference
β_x	98.8 ± 16.2	102.6 ± 15.0	-3.82 ± 3.87
β_t	90.4 ± 14.1	98.9 ± 8.82	-8.50 ± 6.89
β_{tx}	95.1 ± 7.51	99.4 ± 6.13	-4.32 ± 2.74

Simulation results (preliminary) - **non-monotone**

Relative bias (%)

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	MNI	FCS OIM	Difference
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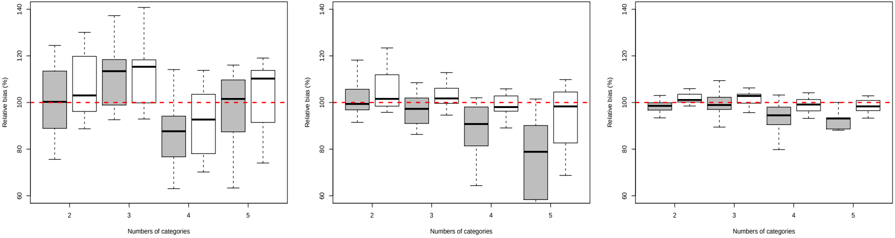
Mean square error (MSE): similar for MNI and FCS OIM.

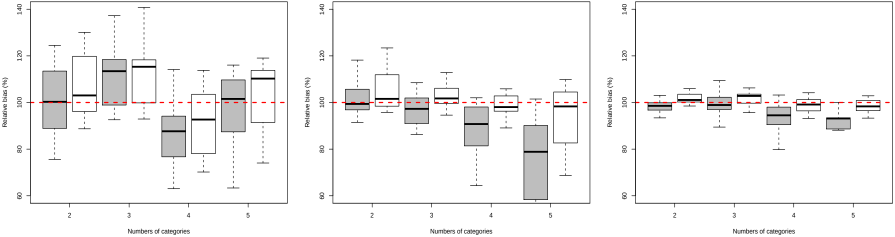
Simulation results (preliminary) - **non-monotone**

Number of levels K

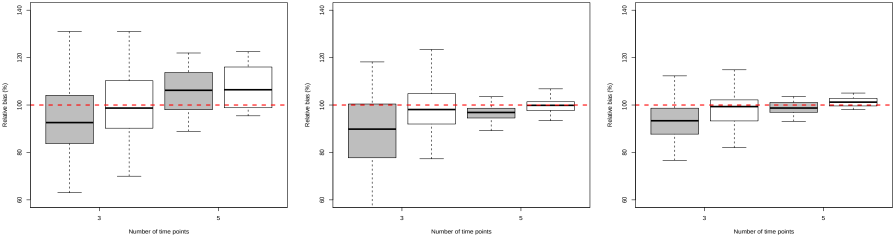


Simulation results (preliminary) - **non-monotone**

Number of levels K

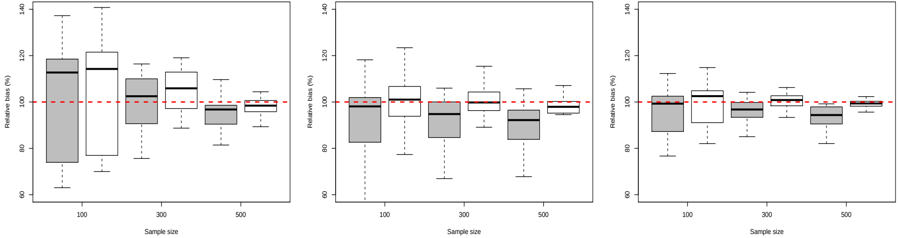


Number of time points T



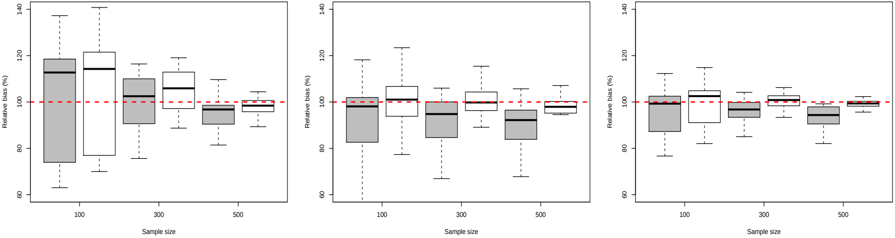
Simulation results (preliminary) - **non-monotone**

Sample size

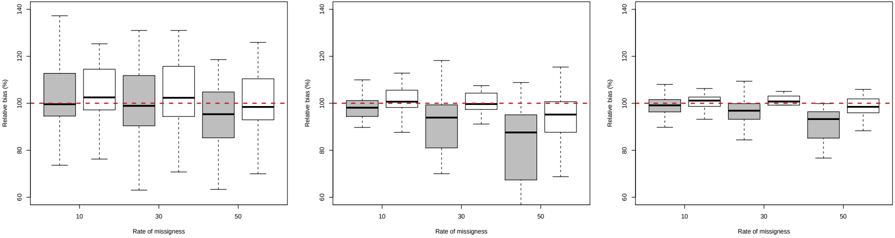


Simulation results (preliminary) - **non-monotone**

Sample size



Rate of missingness



Conclusions - **non-monotone**

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 Conclusions (preliminary) - non-monotone

Conclusions - **non-monotone**

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- The effects of simulation parameters on the RB are similar than those found for the monotone case.

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MSE

- MNI and FCS OIM were similar

Conclusion - General

Monotone: Advisable to impute missing ordinal data using appropriate method.

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Monotone: Advisable to impute missing ordinal data using appropriate method.

Non-monotone: No great differences were observed between the two methods (To be confirmed).

Thank you.